I congratulate Doctor Hoag on his perseverance and his patience in so thoroughly trying out this work before presenting it to you today, also allowing the judgment of others to assist him in his final conclusions.

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HAROLD BRUNN, M. D. (384 Post Street, San Francisco).—Doctor Hoag is to be congratulated on developing a new incision which gives a great deal of room and easy working space in the upper abdomen on either the right or left side. There has been a tendency toward transverse abdominal incisions for some time. This type of incision seems to have the habit of becoming popularized and then disappearing from view and being rediscovered.

The incision of Doctor Hoag's, however, is somewhat different and does give access to a region which is very difficult to reach with the ordinary longitudinal incision through the right rectus.

It is not unusual in abdominal operations, when an exploration has been made through the right rectus, to find it necessary to make a transverse incision either to the left or right in order to obtain more room. Doctor Hoag, however, has developed this operation to its greatest extent and shows how, if properly made and extensive enough in the back, a longitudinal incision is not necessary. I am sure that this method of approach should always be considered when any mass is to be removed either from the right or from the left side, especially those that may be retroperitoneal or for large tumors involving either kidney.

The pictures which illustrate the article are exceedingly good and should be carefully studied in order that the incision developed by Doctor Hoag should be used as described.

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JOHN B. DEC. M. SAUNDERS, F. R. C. S. (University of California Medical School, San Francisco).—The approach devised by Dr. Carl Hoag for resection of cancers involving the colonic flexures is a distinct and valuable contribution to surgery. There can be little question that an approach of this type is, in view of its directness, the most logical procedure for exposure of the flexures, which structures are deeply placed in the flanks; in the wide hollows on either side of the prominent bodies of the lumbar vertebrae. The problem raised by such an approach is the question as to whether or not the essential nerve supply of the musculature can be preserved in order to maintain the integrity of the abdominal parieties. Our conception of the course and distribution of the intercostal nerves has undergone considerable changes from those which are to be found in the standard textbooks of anatomy. Doctor Hoag has mentioned the recent work of Davis, Gladstone and Stibbe on the intercostal nerves, which merits the close attention of all those who are interested in problems of abdominal approach. We have been able to confirm for the most part the findings of these authors, findings which indicate that this route is anatomically sound. There can be little question that an approach of this type secures the most adequate exposure of the colon that it is possible to obtain. The position of the patient is an additional advantage in that the abdominal contents are carried out of the way and do not obstruct the field.

The dictum that the surgery of carcinoma of the large bowel is dependent upon its lymph drainage and vascular supply has now become axiomatic. An approach which enables us to reach with ease the vessels of the colon, to mobilize the bowel and to perform wide resection of the lymph bearing area is a decided advantage. The value of this route is nowhere better illustrated than in cases of carcinoma of the splenic flexures. It is well known that recurrences after resection of this flexure invariably occur in the region of the hilum of the spleen. The usual anterior type of approach renders it difficult to deal with this area, whereas by means of the postero-lateral route described by Doctor Hoag this region is readily accessible.

Doctor Hoag is to be congratulated on the approach which he has devised as it presents so many valuable features in dealing with malignant disease affecting the colon. Exposures of this type warrant a more extensive use than has been accorded to them in the past.

ADRENAL ENDOCRINOPATHIES IN CHILDHOOD*

By H. CLARE SHEPARDSON, M.D.
San Francisco

DISCUSSION *by Rieta C. Hough, M. D., San Diego; Frank Hinman, M. D., San Francisco; Francis Scott Smyth, M. D., San Francisco.*

ALTHOUGH Eustachius discovered the adrenal glands in 1563, their importance was not suspected until nearly three hundred years later when Addison, in 1855, showed their relation to the disease known by his name. In the human there are two adrenal glands, which lie embedded in the fat above the kidney on either side. These small triangular or cocked-hat shaped bodies are composed of two parts, cortex and medulla, which, although anatomically united, are morphologically and embryologically distinct structures. The cortex is derived from the mesothelium of the Wolffian ridge, as are also the ovary and testis, while the medulla takes its origin from the intraneural ectoderm that gives rise to the nerve cells of the sympathetic ganglia. In the higher animals the anatomical contiguity of these derivations of the interrenal and chromaffin systems is so intimate that they are fused into a united gland. However, accessory adrenals or aberrant masses of adrenal tissue are met with frequently. These are often quite small, and are found usually in one of four chief locations, in the kidney along the suprarenal vein, near the solar plexus and the inferior surface of the liver, about the uterus, ovary and tube, and in the spermatic cord and corpus Highmori.

ADRENAL GLANDS A FAVORITE FIELD OF STUDY FOR THE EXPERIMENTAL PHYSIOLOGISTS

Of all the members of the ductless glandular apparatus, the adrenals have been the happy hunting grounds de luxe for the experimental physiologist. Yet, despite the amazing ingenuity of these indefatigable workers, the present state of our knowledge regarding the physiology of the adrenal is still far from satisfactory. Extirpation of one adrenal has little or no apparent effect, although when both are removed death speedily ensues. While much controversy has surrounded the question as to which portion of the adrenal body is essential to life, it has now been demonstrated that death is due to removal or destruction of the cortical substance and not to loss of the medulla. Unfortunately, "up to the present time it has not been possible to produce experimentally any well characterized symptoms associated with adrenal insufficiency. The operator either leaves so much of the gland that the animal survives indefinitely in good health, or takes away so much that it dies quickly, as it would have done if the glands had been totally excised." (Stewart.) No intermediate state between health and death has been achieved. As a result many details of the physiology of the adrenals are still unknown or

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contradictory. However, with the isolation of an active cortical hormone (or hormones) by Hartman, and by Swingle and Pfiffner, a new chapter in the physiology of these glands, particularly the "indispensable to life" portion, is being written.

ADRENAL GLAND FUNCTION FREQUENTLY MISINTERPRETED

Heretofore, all manner of conditions have been ascribed to disturbance in function of the adrenal glands, particularly insufficient activity, mostly as a result of a slightly lowered systolic blood-pressure. It is a simple matter to fasten the label of adrenal deficiency on to any individual who feels somewhat below par, and whose blood-pressure ranges between 100 and 110 millimeters of mercury. Thus we have seen the hypoadrenal constitution, the hypothetical hypoadrenalism associated with infectious diseases, and various and sundry intoxications and dyspepsias. It has been inferred that many or all of these so-called hypoadrenal states are mild, incomplete forms of Addison's disease, and this in spite of the fact that experimental physiology affords no basis for the view that loss of the epinephrin secretion of the medulla is in itself important. Stewart has shown that arterial hypotension is not caused even when the epinephrin output is totally suppressed.

No mention will be made of the multitude of conditions at one time or another ascribed to adrenal disturbance, when the evidence for such relationship is either faulty, dubious or purely imaginative. There are, however, a few clinical syndromes in which adrenal lesions of unimpeachable character have been repeatedly discovered. And even in these maladies, where the adrenal pathology is beyond question, the functional interpretation of the clinical manifestation is often difficult, doubtful or impossible.

ANOMALIES OF THE ADRENAL BODIES

Anomalies of the adrenal bodies have little clinical significance. Usually they are found associated with cerebral defects. Zander discovered abnormally small adrenals in forty-two cases of hemicephaly. Hypoplasia of the adrenal cortex has accompanied anencephalus and may be associated with pituitary anomalies. In Czerny's five cases of congenital hydrocephalus, the medullary portion of the adrenals was entirely lacking. In Elliott and Armour's case of anencephaly the adrenal cortex was absent. These congenital malformations are extremely unusual, and so bizarre that it is impossible at present to determine whether the cerebral and adrenal anomalies are merely coincidental, or whether the brain abnormalities are in some peculiar way dependent on the adrenal defects.

ACUTE ADRENAL INSUFFICIENCY

Acute adrenal insufficiency, with symptoms quite different from those of Addison's disease, occurs in the so-called suprarenal apoplexy of small children. Virchow first called attention to the condition. The characteristic symptoms are sudden onset with fever, violent pain in the hypochondrium radiating to the loin, later tympanites, collapse and death within forty-eight hours of the onset of the attack. Glauzmanns' review, in 1933, refers to this condition, which in small children is frequently accompanied by cutaneous purpura, as the Waterhouse-Friderichsen syndrome. As Osler pointed out years ago, the picture presented by acute hemorrhagic adrenalitis resembles quite closely that of acute pancreatitis. However, the degree of shock in the former is more profound than that encountered in acute pancreatitis, or in peritonitis or ileus.[2] The destructive hemorrhage may occur in adrenals that were previously healthy, or in those that were the seat of disease with or without symptoms. In the searching for etiological factors responsible for this condition, a great number of theories have been advanced. Kempf[3] calls attention to the developmental changes taking place in the adrenals, both in intrauterine life and particularly in the first twelve months after birth. From the first month to the twelfth month postpartum, there occurs a capillary hyperemia of the inner layer of the adrenals which at birth consists mostly of cortex, except for small complexes of medullary cells dispersed about the veins. After the second month this hyperemia is marked and there occurs fatty, vacuolar and colloid degenerative changes in the cortical cells, the atrophic cells being replaced by the medullary cells which ever increase in number as if being able to withstand the pressure of the hyperemia to which the cortical cells succumb. It is this hyperemia and destruction which Kempf claims is the most important predisposing factor in adrenal hemorrhage in the young.

Many clinicians have assigned the dominant rôle in the production of symptoms to variations in the epinephrin output. It is the general impression that a marked diminution of epinephrin is of serious import, its total suppression a calamity. However, like many other clinical impressions, these are not supported by experimental data; for, as has been mentioned, there is no evidence to show that diminution in the ordinary rate of output of epinephrin can give rise to symptoms. Yet it can only with difficulty be presumed that the lethal outcome results from destruction of the cortex, for fatal cases have been reported in which the cortex was morphologically well preserved.

Diagnosis during life is very difficult. The presence of severe abdominal symptoms with few or no physical manifestations, profound asthenia and gradual decline of blood pressure should suggest the presence of acute hemorrhagic adrenalitis. The leukocyte count is apt to be high and there may be a marked hyperpyrexia.

Treatment of bilateral suprarenal apoplexy has met with little success. Surgery offers no help.[2] The administration of large amounts of sodium chlorid, together with cortical extract, sedatives and even adrenalin, seem only to postpone the fatal outcome.

CHRONIC ADRENAL INSUFFICIENCY

Chronic adrenal insufficiency, first described by Thomas Addison, in 1855, results in a symptom complex universally associated with the name of its discoverer. While Addison's disease is pre-

ponderantly one of the fourth, fifth and sixth decades, it may occur at any age. Osler described a congenital case in which the child lived eight weeks. The youngest patient in Rowntree's[4] series of approximately three hundred cases was fourteen years of age. Morabito,[5] in his article on Addison's disease in infancy, remarks that the disease is rare in infancy, probably because the suprarenal glands possess special resistance to tuberculous infection and to other processes that lead to this disease.

It is generally accepted that in spite of the fact that the condition has not been produced experimentally, a hyposecretion of both the medulla and the cortex of the adrenal glands is the causal factor of the disease (although the recent suggestion by Wilder[6] that Addison's disease may have to be considered as resulting from disturbed function of the anterior hypophysis, as well as the adrenals, may prove extremely important). While any pathologic lesion which destroys the suprarenal bodies will produce the characteristic syndrome in whole or in part, tuberculosis is, of course, the commonest cause. It is interesting, however, that only one third of Rowntree's patients had clinical evidence of tuberculosis and that Addison's disease is extremely uncommon in patients in sanitariums. In Lewin's[7] series of five hundred cases, tuberculosis was present in about one-third. It should be added that atrophy or hypoplasia of the adrenals is a more common cause of this disease than has heretofore been supposed, although such pathologic changes are only rarely encountered in childhood.

The disease is characterized clinically by marked asthenia, resulting from both muscular and vascular weakness, continued and extremely low blood-pressure, a characteristic brown or chocolate colored pigmentation of the skin and mucous membranes, especially of the mouth, gastrointestinal symptoms including diarrhea, vomiting, pain in the epigastrium and later complete anorexia, and loss of memory, delirium, dizziness, tinnitus and other nervous and mental manifestations, such as constant apathy, depression, insomnia or rarely, increased tendency to sleep. The temperature is usually subnormal; there is no anemia except that resulting from such complicating diseases as tuberculosis or cancer. The blood sugar is low. Other laboratory procedures give little aid in diagnosis; although ordinarily little trouble is experienced, for the picture is one which can scarcely be confused with any other clinical syndrome.

Until quite recently the treatment of Addison's disease has been rather a thankless task. Even now the course of the disease usually is progressively downward, although occasionally a patient seems to recover spontaneously; remissions may occur, persisting for a number of weeks, months or even years. Until three or four years ago progress toward remedy of this malady was negligible in spite of the heroic efforts made to administer the only active extract of the adrenals then known, epinephrin, orally, rectally and by hypodermic. No convincing improvement ensued from medullary adrenal therapy. More recently, however, improvement seemingly has followed the administration of the adrenal cortical extracts of Swingle and Pfiffner, and of Hartman. It is as yet premature to forecast the ultimate scope of adrenal cortex therapy in Addison's disease, but it is obvious that the isolation of this hormone constitutes one of the major advances in endocrinology. Lisser, Taylor and Leet,[8] in summarizing the accomplishments of cortical extracts in the treatment of Addison's disease, state that while enough persons who would have succumbed almost certainly within twenty-four hours have been revived by cortical extracts, to banish any doubt as to the specificity or potency of this hormone, further purification and concentration are needed. The expense involved in administering adequate doses is prohibitive except in isolated instances. Cheaper methods of extraction are most desirable, so that these preparations can receive the clinical application they deserve. During crisis, daily injections of 50 to 100 cubic centimeters of this hormone, as it now exists, are required. This tremendous dosage may be necessary for several days, although subsequently the patients' health may be maintained with as little as 2 cubic centimeters daily. In most instances, however, the maintenance dose varies from 3 to 5 cubic centimeters daily. Consequently, the actual use of this hormone has been restricted to the very few who can afford it, or to such clinics as are richly endowed.

It is altogether probable that the suggestion made by Harrap that a high salt intake may markedly reduce the need of cortical extract, except in times of crises, will aid in solving to a certain extent the problem of costliness. Sodium chlorid should be given daily in doses of 1 to 7 grams.

Finally, it should be added that once the hormonal deficiency is adequately replaced, the problem of the chronicity and of the tuberculosis must still be faced.

MEDULLARY TUMORS

Inasmuch as the anlage of the suprarenal medulla lies in the sympathetic ganglions, which in turn are derived from the neural crest, medullary growths are of neuroblastic origin. Two forms are usually encountered: the type described by Hutchinson and the one depicted by William Pepper (III). They usually occur during infancy or early childhood.

The Hutchinson variety is characterized by metastatic involvement of the orbit, skull and long bones. Ecchymosis of one or both eyelids, soon followed by exophthalmos, is a frequent occurrence. The discoverer of this peculiar syndrome originally reported thirteen cases in children from three months to nine years of age.

The Pepper type is characterized by its rapid growth and its tendency to metastasize to the liver, lungs or abdominal lymph-nodes. The liver especially may be diffusely involved, the abdomen becoming greatly distended, but without ascites or jaundice.

In a third and very rare clinical type of neuroblastoma, the symptoms of severe secondary anemia develop. The case may be mistaken for one of pernicious anemia.

Mention is made of these three types of medullary tumors simply for the sake of completeness. None of them result in endocrinopathies.

The paragangliomas or chromaffin cell tumors are the most significant of the medullary group. It is with these rare tumors that nonnephritic paroxysmal, or intermittent, hypertension has been reported. This clinical syndrome (which is characterized by recurrent attacks of marked hypertension, although in the interim the blood-pressure may remain quite normal), is due in all probability directly or indirectly to the excessive secretion of epinephrin or some allied compound. The tumors are usually benign and do not produce cachectic states. Wiesel[9] called attention to the vascular sclerosis due to this type of tumor in a child aged two years. A few instances of cure resulting from removal of the tumor have been reported.

"In a study of the cases reported in the literature of tumors of the suprarenal gland, the complexity of the whole problem is especially striking. There are many cases in which the clinical and pathologic data seem to indicate involvement of some particular portion and even some type of cell, and the diagnosis is definite and clean cut. In other instances the complexity of the clinical picture would seem to point to involvement of both the medulla and cortex."[10]

SECRETIONS OF THE SUPRARENAL CORTEX INFLUENCE THE DEVELOPMENT OF THE SEXUAL SYSTEM

There can be no reasonable doubt that the secretions of the suprarenal cortex exert a powerful influence upon the development of the sexual system. Numerous cases of tumor of the suprarenal cortex have been reported, uniformly associated with marked changes in bodily development, and anomalous sex manifestations. Depending on the age in which the disease arises, the glandular manifestations vary. Thus, if the influence of the cortical growth with its excessive function begins during prenatal life pseudohermaphroditism results, while in the group in which the hyperfunction originates in early childhood, prior to puberty, the syndrome of pubertas praecox develops. A third type, occurring only in the adult female, is associated with virilism. Several instances of pseudohermaphroditism resulting from or at least associated with bilateral hyperplasia of the suprarenals or with ectopic suprarenal rests, have been reported. It occurs more frequently in the female and consists in a marked overgrowth of the clitoris with concomitant suppression of growth of the uterus and ovaries. However, we have seen recently at the University of California Hospital what was supposed to be a boy of two years of age, who externally had what seemed to be a small penis, with the urethra in the normal position, and below it an empty scrotum. An exploratory laparotomy revealed the presence of ovaries, tubes and uterus. At autopsy this patient was found to have a bilateral suprarenal cortical hyperplasia.

No satisfactory treatment has been devised as yet, although the recent interest in adrenal surgery may, by partial adrenalectomy, provide an opportunity for normal femininity to develop by removing the masculinizing impulse.

TUMORS OF THE SUPRARENAL CORTEX

Tumors of the suprarenal cortex developing in childhood produce a premature growth and ripening of the entire organism. A large proportion of these cortical tumors have been found in females. However, Lisser,[11] after carefully searching the literature, found eight unquestionable instances of adrenal cortical tumors in boys causing sexual precocity. After reporting a ninth case, and the only one of this kind in which the tumor was successfully removed, he adds that two additional cases very likely may fall in this category. Freedman[12] has adequately discussed the differential diagnosis from pineal tumors and tumors of the gonads. The former (pineal tumors) always occur in boys and uniformly result in excessive height and rapid physical development, whereas the latter in most instances are found in girls. In fact, most of the cases of precocious puberty in girls have been found due to ovarian growths, probably granulosa cell tumors. Hyperfunction of the internal genitalia, with consequent abnormally early menarche, is usually associated with this type of tumor. Premature onset of the menstrual cycle points to pathologic involvement of the ovaries; suprarenal cortical tumors are more apt to produce hypertrophy of the external genitalia. In addition, there seems to be a "tendency to the development of the male at the expense of the female characters in the girls (virilismus), and an intensification of the male characters in the boy (pubertas praecox virilis)." Girls are masculinized, as is exemplified by the growth of beard and mustache, hair on the chest, upper thighs and abdomen and by hypertrophy of the clitoris, deepening of the voice and a masculine bodily configuration. Menstruation is usually absent, although in certain cases in which cortical tumors have been found there has been early female sexual development with the onset of menstruation in early childhood.

Boys of four or five may have the external genitalia of the adult, as in Lisser's case, with abundant hair on the mons pubis, in the axilla and on the upper lip and chin.

The accelerated development is not restricted to the sexual domain or secondary sex characters, but is accompanied by advanced ossification, dentition, bone growth, unusual muscular strength, and adiposity. The development of the psyche does not, as a rule, keep pace with the rapid bodily growth and maturity in contrast to the astonishing maturity of thought, mind and speech said to be associated with the rare instances of macrogenitosomia praecox resulting from pineal tumors.

It is the recognized association of hirsutism and virilism with adrenal cortical tumors which has resulted in the suggestion that yet another hormone may be secreted by the cortex, since excesses of the cortical hormone as it is at present known can hardly be held responsible for this syndrome. As a matter of fact, our present knowledge of the physiology of the adrenal glands is in many respects quite primitive. Undoubtedly new researches

will, in time, clarify the present chaotic mass of information now at our disposal. For the present, however, it is felt that a brief review of this type should concern itself only with variations from the normal which can be ascribed with reasonable certainty to abnormal function of the adrenal glands. Finally, it should be mentioned that in as much as consideration has been given only to those conditions for which we have rather definite evidence that alteration in activity of either the medulla or cortex of the adrenals is the morbific factor, no attempt has been made to analyze the rather voluminous literature which has accumulated on the subject of adrenal dysfunction.

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DISCUSSION

RIETA C. HOUGH, M. D. (1212 Medico-Dental Building, San Diego).—Doctor Shepardson has covered the subject so thoroughly that relatively little is left to say. However, there are one or two points which may be noted.

The adrenals contain more vitamin C in the form of "ascorbic acid" or, as it has more recently been called, "cevitamic acid," than any other gland in the body. Experiments on rats indicate that scurvy is a dysfunction of the adrenals. Probably the improvement in patients with malnutrition who have been fed adrenal compound may have been due as much to the ascorbic content as to the gland itself.

The relation between the adrenals and sodium metabolism has definitely been brought out, patients with Addison's disease are greatly improved by the addition of large amounts of sodium chlorid to their diet, and the dosage of cortin required varies with the sodium chlorid intake. Recently it has been reported that adrenalectomized animals have been kept alive indefinitely by the giving of sodium chlorid and sodium bicarbonate, or sodium chlorid and sodium citrate without the use of cortin; if this proves satisfactory in humans, it will be a boon to the patients with Addison's disease.

The suggested use of cortin in cases of bronchial asthma, glaucoma, mastoiditis, low blood pressure, generalized weakness, etc., indicates that our knowledge of adrenal function is limited, and that the study of this gland still offers a large field for research.

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FRANK HINMAN, M. D. (384 Post Street, San Francisco).—These conditions, which have been so fully described by Doctor Shepardson, open up an entirely new field in surgery. The great possibilities in the surgical correction of pseudohermaphroditic anomalies were presented recently in a striking manner by Doctor Young, who has done pioneer work in this field.

There are two aspects for consideration: First, discovery and correction of the endocrine disturbance; second, surgical repair of the anomaly of development which this disturbance has produced. Confusion will arise in the correct interpretation of the endocrine disturbance, because of the close interrelations of the activities of the pineal, pituitary and thymus glands, and the gonads with those of the adrenals. Cryptorchids occasionally are found to be pseudohermaphrodites. The sexual syndromes arise from the adrenal, through changes in the normal activity of the interrenal component (cortex). When hyperactivity occurs in fetal life (usually in females), it produces pseudohermaphroditism; when in fancy (usually in males), it produces precocity; and when it occurs after puberty (usually in females) hirsutism and masculinism result. The pathologic change in the adrenal gland, associated with these various syndromes, is an increase in the number of cortical cells either in the form of a circumscribed adenoma, of diffuse adenomatous nodules, or of uniform hypertrophy. Sometimes these changes cannot be recognized by the surgeon even after full exposure of the glands. The circumscribed adenomas, as in Lisser's case, will displace the kidney downward and outward, a well-marked characteristic of adrenal tumors which is demonstrable pyelographically. The other forms of cortical hyperactivity give no urologic indication—no tumor is demonstrable, pyelograms are normal, and the diagnosis must be made on the strength of the genito-adrenal syndrome alone. Exploratory operation is indicated. If there has been no clinical evidence of the side on which a possible adenoma may be present, and exposure of one gland reveals apparently normal tissue, it is well not to close the wound until after the other gland has been inspected; because, if it also reveals no adenoma and is normal in appearance, the indication is for partial resection of both glands. In two such instances in my own experience, subsequent microscopic study of the resected portions revealed hypertrophic nodules as the cause of the cortical hyperactivity. This is just one of the types of surgery applicable to the first aspect of the problem: correction of the primary endocrine disturbance. It may be all that is required surgically.

The many interesting types of surgery applicable to the repair of the various maldevelopments caused by excess hormonal activity and deficiency cannot be more than mentioned in this discussion. This second aspect of the problem, however, is as important as the first. The remarkable case of Doctor Young's patient with true hermaphrodism (both testis and ovary), in whom masculine characteristics were made predominant by removal of the female structures and repair of the male, is an example of what can be done surgically in this new field.

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FRANCIS SCOTT SMYTH, M. D. (University of California Hospital, San Francisco).—The great temptation to let fancy roam when discussing problems of endocrinology is altogether too frequent in medical literature. Doctor Shepardson has, however, clearly presented only what is known, and has shown great restraint in discussing the confusion of clinical application. I dare say that it might have been easier for him to have limited his treatise to a lengthy review of experimental work, or to have indulged in a flight of ideas in discussing detailed case studies. However, he has avoided both extremes. Those of us who have seen some of the patients to whom he refers, and have likewise benefited from Doctor Lisser's pioneer interest in the field, can realize how valuable is persistent study linked with healthy skepticism.